```
=> file caplus; d que l1
FILE 'CAPLUS' ENTERED AT 14:54:43 ON 16 JUN 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)
```



```
FILE COVERS 1907 - 16 Jun 2005  VOL 142 ISS 25
FILE LAST UPDATED: 15 Jun 2005  (20050615/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.


L1            10 SEA FILE=CAPLUS ABB=ON  PLU=ON  "BALABAN N"/AU


=> file medline; d que l3; d que l6
FILE 'MEDLINE' ENTERED AT 14:54:55 ON 16 JUN 2005

 FILE LAST UPDATED: 15 JUN 2005 (20050615/UP).  FILE COVERS 1950 TO DATE.

 On December 19, 2004, the 2005 MeSH terms were loaded.

 The MEDLINE reload for 2005 is now available.  For details enter HELP
 RLOAD at an arrow promt (=>).  See also:

    http://www.nlm.nih.gov/mesh/
    http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

 OLDMEDLINE now back to 1950.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2005 vocabulary.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L2            21 SEA FILE=MEDLINE ABB=ON  PLU=ON  "BALABAN N"/AU
L3             8 SEA FILE=MEDLINE ABB=ON  PLU=ON  L2 AND STAPH?



L5            12 SEA FILE=MEDLINE ABB=ON  PLU=ON  "BALABAN NAOMI"/AU
L6            10 SEA FILE=MEDLINE ABB=ON  PLU=ON  L5 AND STAPH?
```

```
=> s l3 or l6
L12         18 L3 OR L6

=> file embase; d que l8
FILE 'EMBASE' ENTERED AT 14:55:14 ON 16 JUN 2005
COPYRIGHT (C) 2005 Elsevier Inc. All rights reserved.

 FILE COVERS 1974 TO 9 Jun 2005 (20050609/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L7            42 SEA FILE=EMBASE ABB=ON  PLU=ON  "BALABAN N"/AU
L8            21 SEA FILE=EMBASE ABB=ON  PLU=ON  L7 AND STAPH?


=> file biosis; d que l10
FILE 'BIOSIS' ENTERED AT 14:55:26 ON 16 JUN 2005
Copyright (c) 2005 The Thomson Corporation

FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 10 June 2005 (20050610/ED)

FILE RELOADED: 19 October 2003.


L9            45 SEA FILE=BIOSIS ABB=ON  PLU=ON  "BALABAN N"/AU OR "BALABAN
                 NAOMI"/AU OR "BALABAN NAONU"/AU
L10           20 SEA FILE=BIOSIS ABB=ON  PLU=ON  L9 AND STAPH?


=> file wpix; d que l11
FILE 'WPIX' ENTERED AT 14:55:33 ON 16 JUN 2005
COPYRIGHT (C) 2005 THE THOMSON CORPORATION

FILE LAST UPDATED:          13 JUN 2005      <20050613/UP>
MOST RECENT DERWENT UPDATE:     200537        <200537/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
    PLEASE VISIT:
 http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
    http://thomsonderwent.com/coverage/latestupdates/           <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER
    GUIDES, PLEASE VISIT:
    http://thomsonderwent.com/support/userguides/               <<<

>>> NEW! FAST-ALERTING ACCESS TO NEWLY-PUBLISHED PATENT
    DOCUMENTATION NOW AVAILABLE IN DERWENT WORLD PATENTS INDEX
```

FIRST VIEW - FILE WPIFV.
FOR FURTHER DETAILS: http://www.thomsonderwent.com/dwpifv <<<

>>> THE CPI AND EPI MANUAL CODES HAVE BEEN REVISED FROM UPDATE 200501.
PLEASE CHECK:
http://thomsonderwent.com/support/dwpiref/reftools/classification/code-revision/
FOR DETAILS. <<<

L11 4 SEA FILE=WPIX ABB=ON PLU=ON "BALABAN N"/AU

=> dup rem l12 l1 l8 l10 l11
FILE 'MEDLINE' ENTERED AT 14:55:49 ON 16 JUN 2005

FILE 'CAPLUS' ENTERED AT 14:55:49 ON 16 JUN 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'EMBASE' ENTERED AT 14:55:49 ON 16 JUN 2005
COPYRIGHT (C) 2005 Elsevier Inc. All rights reserved.

FILE 'BIOSIS' ENTERED AT 14:55:49 ON 16 JUN 2005
Copyright (c) 2005 The Thomson Corporation

FILE 'WPIX' ENTERED AT 14:55:49 ON 16 JUN 2005
COPYRIGHT (C) 2005 THE THOMSON CORPORATION
PROCESSING COMPLETED FOR L12
PROCESSING COMPLETED FOR L1
PROCESSING COMPLETED FOR L8
PROCESSING COMPLETED FOR L10
PROCESSING COMPLETED FOR L11
L13 35 DUP REM L12 L1 L8 L10 L11 (38 DUPLICATES REMOVED)
ANSWERS '1-18' FROM FILE MEDLINE
ANSWERS '19-25' FROM FILE CAPLUS
ANSWERS '26-28' FROM FILE EMBASE
ANSWERS '29-31' FROM FILE BIOSIS
ANSWERS '32-35' FROM FILE WPIX

=> d ibib ed ab l13 1-31; d ibib ab abex l13 32-35

L13 ANSWER 1 OF 35 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2005004884 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 15629527
TITLE: RNAIII-inhibiting peptide improves efficacy of clinically used antibiotics in a murine model of **staphylococcal** sepsis.
AUTHOR: Giacometti Andrea; Cirioni Oscar; Ghiselli Roberto; Dell'Acqua Giorgio; Orlando Fiorenza; D'Amato Giuseppina; Mocchegiani Federico; Silvestri Carmela; Del Prete Maria Simona; Rocchi Marco; **Balaban Naomi**; Saba Vittorio; Scalise Giorgio
CORPORATE SOURCE: Institute of Infectious Diseases and Public Health, Universita Politecnica delle Marche, Ancona, Italy.
SOURCE: Peptides, (2005 Feb) 26 (2) 169-75.
Journal code: 8008690. ISSN: 0196-9781.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20050105
Last Updated on STN: 20050202
ED Entered STN: 20050105
Last Updated on STN: 20050202
AB RNAIII-inhibiting peptide (RIP, YSPWTNF-NH2) is a quorum-sensing peptide inhibitor that prevents **Staphylococcus** aureus toxin production and biofilm formation. A mouse sepsis model was used to test the efficacy of RIP alone or in combination with conventional antibiotics in suppressing S. aureus-induced sepsis. Mice were injected intravenously with 3.0x10(6)CFU of S. aureus ATCC 25923 or with 3.0x10(6)CFU of S. aureus strain Smith diffuse. All animals were randomized to receive intravenously isotonic sodium chloride solution as a control, or 20 mg/kg RIP alone or combined with 20 mg/kg cefazolin, 10 mg/kg imipenem, or 10 mg/kg vancomycin immediately or 6 h after bacterial challenge. Main outcome measures were bacteremia and lethality. All compounds reduced lethality when compared to controls. Although, in general combined-treated groups had significant lower bacterial counts when associated to singly-treated groups only the combination between RIP and vancomycin with respect to cefazolin gave a statistically significant decrease in the lethality rate. Lowest lethality rates (10%) and bacteremia (<10(2)CFU/ml) were obtained when RIP was administered in combination with vancomycin. Because RIP can be synergistic with current antibiotic therapies and help to reduce S. aureus exotoxins production, it can be considered a promising agent to associate with antibiotics for further clinical research into treatment of sepsis.

L13 ANSWER 2 OF 35 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2004187687 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14726534
TITLE: Quorum sensing in **Staphylococci** is regulated via phosphorylation of three conserved histidine residues.
AUTHOR: Gov Yael; Borovok Ilya; Korem Moshe; Singh Vineet K; Jayaswal Radheshyam K; Wilkinson Brian J; Rich Stephen M; **Balaban Naomi**
CORPORATE SOURCE: Department of Human Microbiology, Sackler School of Medicine, George S. Wise Faculty of Life Sciences, Tel Aviv University, Tel Aviv 69978, Israel.
CONTRACT NUMBER: AI43970 (NIAID)
SOURCE: Journal of biological chemistry, (2004 Apr 9) 279 (15) 14665-72. Electronic Publication: 2004-01-14.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AJ489447; GENBANK-AJ489448; GENBANK-AJ489449; GENBANK-AJ489450
ENTRY MONTH: 200406
ENTRY DATE: Entered STN: 20040416
Last Updated on STN: 20040602
Entered Medline: 20040601
ED Entered STN: 20040416
Last Updated on STN: 20040602
Entered Medline: 20040601
AB **Staphylococcus** aureus cause infections by producing toxins, a process regulated by cell-cell communication (quorum sensing) through the histidine-phosphorylation of the target of RNAIII-activating protein

(TRAP). We show here that TRAP is highly conserved in **staphylococci** and contains three completely conserved histidine residues (His-66, His-79, His-154) that are phosphorylated and essential for its activity. This was tested by constructing a TRAP(-) strain with each of the conserved histidine residues changed to alanine by site-directed mutagenesis. All mutants were tested for pathogenesis in vitro (expression of RNAIII and hemolytic activity) and in vivo (murine cellulitis model). Results show that RNAIII is not expressed in the TRAP(-) strain, that it is non hemolytic, and that it does not cause disease in vivo. These pathogenic phenotypes could be rescued in the strain containing the recovered traP, confirming the importance of TRAP in S. aureus pathogenesis. The phosphorylation of TRAP mutated in any of the conserved histidine residues was significantly reduced, and mutants defective in any one of these residues were non-pathogenic in vitro or in vivo, whereas those mutated in a non-conserved histidine residue (His-124) were as pathogenic as the wild type. These results confirm the importance of the three conserved histidine residues in TRAP activity. The phosphorylation pattern, structure, and gene organization of TRAP deviates from signaling molecules known to date, suggesting that TRAP belongs to a novel class of signal transducers.

L13 ANSWER 3 OF 35 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2004313191 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15215107
TITLE: A chimeric peptide composed of a dermaseptin derivative and an RNA III-inhibiting peptide prevents graft-associated infections by antibiotic-resistant **staphylococci.**
AUTHOR: **Balaban Naomi**; Gov Yael; Giacometti Andrea; Cirioni Oscar; Ghiselli Roberto; Mocchegiani Federico; Orlando Fiorenza; D'Amato Giuseppina; Saba Vittorio; Scalise Giorgio; Bernes Sabina; Mor Amram
CORPORATE SOURCE: Department of Human Microbiology, Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel.
SOURCE: Antimicrobial agents and chemotherapy, (2004 Jul) 48 (7) 2544-50.
Journal code: 0315061. ISSN: 0066-4804.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200409
ENTRY DATE: Entered STN: 20040625
Last Updated on STN: 20040908
Entered Medline: 20040907
ED Entered STN: 20040625
Last Updated on STN: 20040908
Entered Medline: 20040907
AB **Staphylococcal** bacteria are a prevalent cause of infections associated with foreign bodies and indwelling medical devices. Bacteria are capable of escaping antibiotic treatment through encapsulation into biofilms. RNA III-inhibiting peptide (RIP) is a heptapeptide that inhibits **staphylococcal** biofilm formation by obstructing quorum-sensing mechanisms. K(4)-S4(1-13)(a) is a 13-residue dermaseptin derivative (DD(13)) believed to kill bacteria via membrane disruption. We tested each of these peptides as well as a hybrid construct, DD(13)-RIP, for their ability to inhibit bacterial proliferation and suppress quorum sensing in vitro and for their efficacy in preventing **staphylococcal** infection in a rat graft infection model with methicillin-resistant **Staphylococcus** aureus (MRSA) or S.

epidermidis (MRSE). In vitro, proliferation assays demonstrated that RIP had no inhibitory effect, while DD(13)-RIP and DD(13) were equally effective, and that the chimeric peptide but not DD(13) was slightly more effective than RIP in inhibiting RNA III synthesis, a regulatory RNA molecule important for **staphylococcal** pathogenesis. In vivo, the three peptides reduced graft-associated bacterial load in a dose-dependent manner, but the hybrid peptide was most potent in totally preventing **staphylococcal** infections at the lowest dose. In addition, each of the peptides acted synergistically with antibiotics. The data indicate that RIP and DD(13) act in synergy by attacking bacteria simultaneously by two different mechanisms. Such a chimeric peptide may be useful for coating medical devices to prevent drug-resistant **staphylococcal** infections.

L13 ANSWER 4 OF 35 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2004599314 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15572191
TITLE: BisEDT and RIP act in synergy to prevent graft infections by resistant **staphylococci.**
AUTHOR: Domenico Philip; Gurzenda Ellen; Giacometti Andrea; Cirioni Oscar; Ghiselli Roberto; Orlando Fiorenza; Korem Moshe; Saba Vittorio; Scalise Giorgio; **Balaban Naomi**
CORPORATE SOURCE: Cardio Pulmonary Research Institute, Winthrop-University Hospital, SUNY Stony Brook School of Medicine, Mineola 11501, New York, NY, USA.. pdomenico@winthrop.org
SOURCE: Peptides, (2004 Dec) 25 (12) 2047-53.
Journal code: 8008690. ISSN: 0196-9781.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200506
ENTRY DATE: Entered STN: 20041202
Last Updated on STN: 20050608
Entered Medline: 20050607
ED Entered STN: 20041202
Last Updated on STN: 20050608
Entered Medline: 20050607
AB **Staphylococci** are a major cause of infections associated with indwelling medical devices. Biofilm formation on these devices adds to the antibiotic resistance seen among clinical isolates. RNAIII-inhibiting peptide (RIP) is a heptapeptide that inhibits **staphylococcal** pathogenesis, including biofilm formation, by obstructing quorum sensing mechanisms. Bismuth ethanedithiol (BisEDT) also prevents biofilm formation at subinhibitory concentrations. RIP and BisEDT were combined to prevent infections in a rat graft model, using antibiotic sensitive and resistant strains of **Staphylococcus** aureus and **Staphylococcus** epidermidis. BisEDT, RIP, or rifampin, or their combinations reduced the graft associated bacterial load over seven days. BisEDT-RIP was the best combination, reducing bacterial load to undetectable levels. BisEDT-RIP may prove useful for coating medical devices to prevent **staphylococcal** infections.

L13 ANSWER 5 OF 35 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2004313660 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15216467
TITLE: Suppression of drug-resistant **Staphylococcal** Infections by the quorum-sensing inhibitor RNAIII-inhibiting peptide.

AUTHOR: Dell'Acqua Giorgio; Giacometti Andrea; Cirioni Oscar; Ghiselli Roberto; Saba Vittorio; Scalise Giorgio; Gov Yael; **Balaban Naomi**
CORPORATE SOURCE: BalaPharm International, Grafton, Massachusetts, USA.
CONTRACT NUMBER: AI54858 (NIAID)
SOURCE: Journal of infectious diseases, (2004 Jul 15) 190 (2) 318-20. Electronic Publication: 2004-06-24.
Journal code: 0413675. ISSN: 0022-1899.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200408
ENTRY DATE: Entered STN: 20040625
Last Updated on STN: 20040814
Entered Medline: 20040813
ED Entered STN: 20040625
Last Updated on STN: 20040814
Entered Medline: 20040813
AB **Staphylococcus** aureus and S. epidermidis are major causes of infection related to biofilm formed on indwelling medical devices. Such infections are common causes of morbidity and mortality and, because of biofilm resistance to antibiotics, are difficult to treat. The RNAIII-inhibiting peptide (RIP) (YSPWTNF-NH2) inhibits the pathogenesis of **staphylococci** by disrupting bacterial cell-cell communication (known as "quorum sensing"). Using a vascular-graft rat model, we show that RIP, applied locally and systemically, can completely inhibit drug-resistant S. aureus and S. epidermidis biofilms. The present study provides the first direct demonstration that interfering with cell-cell communication by use of a quorum-sensing inhibitor can eliminate medical device-associated **staphylococcal** infections. We suggest that medical devices could be coated with RIP to prevent infections, including those by antibiotic-resistant **staphylococcal** strains.

L13 ANSWER 6 OF 35 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2003263712 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12760879
TITLE: RNA III inhibiting peptide inhibits in vivo biofilm formation by drug-resistant **Staphylococcus** aureus.
AUTHOR: Giacometti Andrea; Cirioni Oscar; Gov Yael; Ghiselli Roberto; Del Prete Maria Simona; Mocchegiani Federico; Saba Vittorio; Orlando Fiorenza; Scalise Giorgio; **Balaban Naomi**; Dell'Acqua Giorgio
CORPORATE SOURCE: Institute of Infectious Diseases and Public Health, Ancona, Italy.
SOURCE: Antimicrobial agents and chemotherapy, (2003 Jun) 47 (6) 1979-83.
Journal code: 0315061. ISSN: 0066-4804.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200310
ENTRY DATE: Entered STN: 20030608
Last Updated on STN: 20031008
Entered Medline: 20031007
ED Entered STN: 20030608
Last Updated on STN: 20031008

AUTHOR(S): **Balaban, N.**; Karahan, Z. C.; Koca, Y.; Guvener, E.
CORPORATE SOURCE: Mikrobiyoloji ve Klinik Mikrobiyoloji Bolumu, Ankara Numune Egitim ve Arastirma Hastanesi, Ankara, Turk.
SOURCE: Mikrobiyoloji Bulteni (2001), 35(2), 211-218
CODEN: MIBUBI; ISSN: 0374-9096
PUBLISHER: Ankara Mikrobiyoloji Dernegi
DOCUMENT TYPE: Journal
LANGUAGE: Turkish
ED Entered STN: 03 Jul 2001
AB Clostridium difficile is the major cause of antibiotic-associated diarrhea and pseudomembranous colitis. The methods to be used in the diagnosis of these diseases are still controversial. In this study we aimed to find the most reliable approach to the diagnosis of C. difficile-associated infections by using two culture [direct inoculation onto cyclocerine-cefoxitin-fructose agar (CCFA) and inoculation onto blood agar after alc. shock enrichment] and two toxin detection methods [enzyme immunoassay (EIA) and immunochromatog. test (ICT)], all of which can be used in all labs. When we evaluated the diarrheal stool samples of 41 patients and normal stool samples of 40 healthy controls and accepted the culture on CCFA as the "gold standard", the sensitivity and specificity of the performed tests were found as follows: Alc. shock enrichment 100% and 100%, EIA 100% and 97%, ICT 100% and 97%, resp. These results show that all of these methods can be used reliably in all labs. and when they are appraised with the clin. findings, the diagnosis of C. difficile associated infections can be made more accurately.

L13 ANSWER 23 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:797953 CAPLUS
DOCUMENT NUMBER: 130:135135
TITLE: H2O2 acts on cellular membranes to generate ceramide signaling and initiate apoptosis in tracheobronchial epithelial cells
AUTHOR(S): Goldkorn, T.; **Balaban, N.**; Shannon, M.; Chea, V.; Matsukuma, K.; Gilchrist, D.; Wang, H.; Chan, C.
CORPORATE SOURCE: Respiratory Signal Transduction, Department of Medicine, Davis School of Medicine, University of California, Davis, CA, 95616, USA
SOURCE: Journal of Cell Science (1998), 111(21), 3209-3220
CODEN: JNCSAI; ISSN: 0021-9533
PUBLISHER: Company of Biologists Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 22 Dec 1998
AB Hydrogen peroxide (H2O2) is an inflammatory oxidant which contributes to the pathogenesis of chronic diseases such as lung injury of the respiratory tract, atherosclerosis and cancer. The mechanisms and target sites of this reactive oxidant are mainly unknown. So far there are opposing reports as to whether reactive oxidants inhibit or promote apoptosis. We activated the death pathway in primary tracheobronchial epithelial (TBE) cells with H2O2 (20-200 μM) and observed the morphol. changes, DNA laddering patterns, and DNA fragmentation associated with apoptosis. Elevation of ceramide with exogenous ceramide analogs was sufficient for apoptosis induction with the same characteristics and in the same time frame. H2O2 induced rapid sphingomyelin hydrolysis to ceramide, the elevation of which paralleled the induction of apoptosis. Furthermore, H2O2 acted directly on TBE cells membrane prepns. devoid of nuclei, stimulating sphingomyelin hydrolysis through a neutral Mg2+

dependent sphingomyelinase (SMase). These data suggest that the formation of ceramide from sphingomyelin in the plasma membrane is a key event in H2O2-induced apoptosis in tracheobronchial epithelial cells.
REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 24 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:97410 CAPLUS
DOCUMENT NUMBER: 114:97410
TITLE: The association of glycosomal enzymes and microtubules: a physiological phenomenon or an experimental artifact?
AUTHOR(S): **Balaban, N.**; Goldman, R.
CORPORATE SOURCE: Dep. Membrane Res., Weizmann Inst. Sci., Rehovot, 76100, Israel
SOURCE: Experimental Cell Research (1990), 191(2), 219-26
CODEN: ECREAL; ISSN: 0014-4827
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 23 Mar 1991
AB Subpellicular microtubules isolated from Trypanosoma brucei parasites were fractionated on a phosphocellulose column, and the trypanosomal p52 microtubule-associated protein was eluted along with two other proteins of 41 and 36 kDa. These proteins were found to be the glycosomal enzymes aldolase (41 kDA) and glyceraldehyde-3-phosphate dehydrogenase (GAPDH, 36 kDa) by enzyme activity, antibody cross-reaction, and N-terminal sequencing. These enzymes were copptd. with tubulin in the presence of taxol, and aldolase had the capacity to polymerize tubulin and cross-link microtubules. Immunolocalization of anti-aldolase and anti-GAPDH antibodies did not show an interaction between these enzymes and the subpellicular microtubules. The question whether the copurifn. of aldolase and the subpellicular microtubules could reflect a physiol. phenomenon or may be an exptl. artifact is discussed.

L13 ANSWER 25 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:17963 CAPLUS
DOCUMENT NUMBER: 112:17963
TITLE: Isolation of a subpellicular microtubule protein from Trypanosoma brucei that mediates crosslinking of microtubules
AUTHOR(S): **Balaban, N.**; Waithaka, H. K.; Njogu, A. R.; Goldman, R.
CORPORATE SOURCE: Dep. Membr. Res., Weizmann Inst. Sci., Rehovot, 76100, Israel
SOURCE: Cell Motility and the Cytoskeleton (1989), 14(3), 393-400
CODEN: CMCYEO; ISSN: 0886-1544
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 21 Jan 1990
AB Subpellicular microtubules were isolated from bloodstream T. brucei parasites by use of a zwitterion detergent. These cold-stable structures were solubilized by a high ionic strength salt solution, and the soluble proteins that contained tubulin along with several other proteins were further fractionated by Mono S cation-exchange column chromatog. Two distinct peaks were eluted containing 1 protein each, which had an apparent mol. weight of 52 kDa and 53 kDa (Mr was determined by SDS-PAGE). Only the 52-kDa
protein showed specific tubulin-binding properties, which were

demonstrated by exposure of nitrocellulose-bound trypanosome proteins to brain tubulin. When this protein was added to brain tubulin in the presence of taxol and GTP, microtubule bundles were formed with regular crosslinks between the parallel closely packed microtubules. The crosslinks were .apprx.7.2 nm apart (center to center). Under the same conditions, but with the 53-kDa protein or without trypanosome-derived proteins, brain tubulin polymerized to single microtubules. It is thus suggested that the unique structural organization of the subpellicular microtubules is dictated by specific parasite proteins and is not an inherent property of the polymerizing tubulin. The in vitro reconstituted microtubule bundles are strikingly similar to the subpellicular microtubule network of the parasite.

L13 ANSWER 26 OF 35 EMBASE
on STN
ACCESSION NUMBER: 2003466187 EMBASE
TITLE: Erratum: Regulation of **Staphylococcus** aureus pathogenesis via target of RNAIII-activating protein (TRAP) (Journal of Biological Chemistry (2001) 276 (2658-2667)).
AUTHOR: **Balaban N.**; Goldkorn T.; Gov Y.; Hirshberg M.; Koyfman N.; Matthews H.R.; Nhan R.T.; Singh B.; Uziel O.
SOURCE: Journal of Biological Chemistry, (8 Jun 2001) Vol. 276, No. 23, pp. 20803.
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Errata
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
ENTRY DATE: Entered STN: 20040105
Last Updated on STN: 20040105
ED Entered STN: 20040105
Last Updated on STN: 20040105

L13 ANSWER 27 OF 35 EMBASE
on STN
ACCESSION NUMBER: 2003458285 EMBASE
TITLE: Erratum: Regulation of **Staphylococcus** aureus pathogenesis via target of RNAIII-activating protein (TRAP) (Journal of Biological Chemistry (2001) 276 (2658-2667)).
AUTHOR: **Balaban N.**; Goldkorn T.; Gov Y.; Hirshberg M.; Koyfman N.; Matthews H.R.; Nhan R.T.; Singh B.; Uziel O.
SOURCE: Journal of Biological Chemistry, (13 Apr 2001) Vol. 276, No. 15, pp. 12476.
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Errata
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
ENTRY DATE: Entered STN: 20031204
Last Updated on STN: 20031204
ED Entered STN: 20031204
Last Updated on STN: 20031204

L13 ANSWER 28 OF 35 EMBASE
on STN
ACCESSION NUMBER: 1999001983 EMBASE
TITLE: An experimental vaccine that targets **staphylococcal** virulence: Response from Balaban.
AUTHOR: **Balaban N.**

CORPORATE SOURCE: N. Balaban, Dept. of Medical Pathology, University of California, Davis, CA 95616, United States
SOURCE: Trends in Microbiology, (1998) Vol. 6, No. 12, pp. 463. Refs: 6
ISSN: 0966-842X CODEN: TRMIEA
PUBLISHER IDENT.: S 0966-842X(98)01423-1
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Note
FILE SEGMENT: 004 Microbiology
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 19990122
Last Updated on STN: 19990122
ED Entered STN: 19990122
Last Updated on STN: 19990122

L13 ANSWER 29 OF 35 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:181752 BIOSIS
DOCUMENT NUMBER: PREV200400185038
TITLE: Target of RNAIII activating protein (TRAP).
AUTHOR(S): **Balaban, Naomi** [Inventor, Reprint Author]; Goldkorn, Tzipora [Inventor]
CORPORATE SOURCE: Davis, CA, USA
ASSIGNEE: The Regents of the University of California
PATENT INFORMATION: US 6689878 20040210
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Feb 10 2004) Vol. 1279, No. 2. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Apr 2004
Last Updated on STN: 7 Apr 2004
ED Entered STN: 7 Apr 2004
Last Updated on STN: 7 Apr 2004
AB The present invention is directed to a protein isolated from S. aureus that is the target of RAP, called TRAP, which is characterized by a molecular weight of about 21 KDa, is capable of being phosphorylated by RAP, and comprises an amino acid sequence of SEQ ID NO:2. In addition, the present invention is directed towards an antibody immunoreactive with TRAP that is preferably a monoclonal antibody or a humanized antibody but may be a polyclonal antibody. The invention provides a method of treating S. aureus infection by administering such a TRAP-inhibiting agent. The invention also features methods for identifying compounds that inhibit TRAP activity and/or inhibit TRAP-RAP interaction.

L13 ANSWER 30 OF 35 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:122979 BIOSIS
DOCUMENT NUMBER: PREV200400126781
TITLE: AFM study of **Staphylococcus** aureus adhesion properties.
AUTHOR(S): Bitler, Arkady [Reprint Author]; **Balaban, Naomi**
CORPORATE SOURCE: Physiology and Pharmacology, Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel
SOURCE: Biophysical Journal, (January 2004) Vol. 86, No. 1, pp. 152a. print.
Meeting Info.: 48th Annual Meeting of the Biophysical

Society. Baltimore, MD, USA. February 14-18, 2004.
Biophysical Society.
ISSN: 0006-3495 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Mar 2004
Last Updated on STN: 3 Mar 2004
ED Entered STN: 3 Mar 2004
Last Updated on STN: 3 Mar 2004
AB Gram-positive bacteria **Staphylococcus** aureus form biofilms through the expression of multiple adhesion molecules, leading to medical-device associated infections. The heptapeptide RIP has been shown to prevent such infections by reducing the level of attachment of bacteria to surfaces. Here we tested the effect of RIP on adhesion properties of single bacterial cell by atomic force microscope (AFM). Atomic force images of single bacteria attached to the polystyrene were acquired in PBS solution in tapping mode. The developed computer program automatically processed images, extracted height profiles around the cell and calculated adhesion characteristics. We found that wild type S. aureus exhibit three different classes of adhesion: weak adhesion with small contact angle, strong adhesion with large contact angle and specific adhesion by pinning centers. When bacteria were treated with RIP, contact angles for weak adhesion remain the same, while contact angles for strong adhesion are smaller and adhesion by pinning centers do not exists. Therefore we show that: (i) RIP changes adhesion of single bacterial cells (ii) RIP eliminates certain types of adhesion; (iii) RIP does not change the weak adhesion mechanisms but reduces strong adhesion mechanisms; (iv) changes of bacterial cells adhesion could be quantified by static characteristic independent on loading rate.

L13 ANSWER 31 OF 35 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:549728 BIOSIS
DOCUMENT NUMBER: PREV200100549728
TITLE: Methods and compositions for the treatment and prevention of **Staphylococcal** infections.
AUTHOR(S): **Balaban, Naomi** [Inventor, Reprint author]; Larrick, James W. [Inventor]; Wright, Susan C. [Inventor]
CORPORATE SOURCE: Davis, CA, USA
ASSIGNEE: Panorama Research, Mountain View, CA, USA; The Regents of the University of California
PATENT INFORMATION: US 6291431 20010918
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Sep. 18, 2001) Vol. 1250, No. 3. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Nov 2001
Last Updated on STN: 25 Feb 2002
ED Entered STN: 21 Nov 2001
Last Updated on STN: 25 Feb 2002
AB Methods and compositions are provided for the treatment of **staphylococcal** infections.

L13 ANSWER 32 OF 35 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2005-123072 [13] WPIX
CROSS REFERENCE: 1999-405112 [34]
DOC. NO. CPI: C2005-040866
TITLE: Preventing or treating bacterial infection caused by any bacteria species in which RNA III-activating protein (RAP) or its target molecule TRAP plays a role in pathogenesis by administering a RAP or TRAP type polypeptide.
DERWENT CLASS: B04 D16
INVENTOR(S): **BALABAN, N**
PATENT ASSIGNEE(S): (BALA-I) BALABAN N
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2005009396	A2	20050203	(200513)*	EN	82

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005009396	A2	WO 2004-US2679	20040130

PRIORITY APPLN. INFO: US 2003-358448 20030203
AB WO2005009396 A UPAB: 20050224
NOVELTY - Preventing or treating bacterial infection, caused by any bacteria species in which RNA III-activating protein (RAP) or its target molecule TRAP plays a role in pathogenesis, comprises administering to a subject a RAP or TRAP type polypeptide to elicit an antibody response.
ACTIVITY - Antibacterial. No biological data given.
MECHANISM OF ACTION - Vaccine; RNA III inhibiting peptide.
USE - The method is useful in preventing or treating bacterial infection caused by any bacteria species in which RNA III-activating protein (RAP) or its target molecule TRAP plays a role in pathogenesis (claimed).
Dwg.0/14
ABEX UPTX: 20050224
ADMINISTRATION - Dosage comprises 0.1-500, preferably 12-100 mg/kg body weight. The composition is administered via oral or parenteral route.

L13 ANSWER 33 OF 35 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 2000-271380 [23] WPIX
DOC. NO. CPI: C2000-082872
TITLE: Novel target of RNAIII activating protein (TRAP) polypeptides and polynucleotides used to identify antagonists and inhibitors for use to treat bacterial infections.
DERWENT CLASS: B04 D16
INVENTOR(S): **BALABAN, N**; GOLDKORN, T; NAHN, R; NAHN, R T
PATENT ASSIGNEE(S): (REGC) UNIV CALIFORNIA; (BALA-I) BALABAN N; (GOLD-I)

GOLDKORN T
COUNTRY COUNT: 85
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000015660	A1	20000323	(200023)*	EN	53
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW					
AU 9964968	A	20000403	(200034)		
EP 1121380	A1	20010808	(200146)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
EP 1188831	A2	20020320	(200227)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
US 2002102271	A1	20020801	(200253)		
US 6689878	B2	20040210	(200413)		
US 6747129	B1	20040608	(200437)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000015660	A1	WO 1999-US21176	19990913
AU 9964968	A	AU 1999-64968	19990913
EP 1121380	A1	EP 1999-952912	19990913
		WO 1999-US21176	19990913
EP 1188831	A2 Div ex	EP 1999-952912	19990913
		EP 2001-122636	19990913
US 2002102271	A1 Provisional	US 1998-100415P	19980915
	Div ex	US 1999-393862	19990910
		US 2001-953780	20010912
US 6689878	B2 Provisional	US 1998-100415P	19980915
	Div ex	US 1999-393862	19990910
		US 2001-953780	20010912
US 6747129	B1 Provisional	US 1998-100415P	19980915
		US 1999-393862	19990910

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9964968	A Based on	WO 2000015660
EP 1121380	A1 Based on	WO 2000015660
EP 1188831	A2 Div ex	EP 1121380

PRIORITY APPLN. INFO: US 1999-393862P 19990910; US 1998-100415P 19980915; US 1999-393862 19990910; US 2001-953780 20010912

AB WO 200015660 A UPAB: 20000725
NOVELTY - Isolated Staphylococcus aureus target of RNAIII activating protein (TRAP) polypeptides are new.
DETAILED DESCRIPTION - A novel isolated TRAP protein (I) has a

Entered Medline: 20031007

AB **Staphylococcus** aureus is a prevalent cause of bacterial infections associated with indwelling medical devices. RNA III inhibiting peptide (RIP) is known to inhibit S. aureus pathogenesis by disrupting quorum-sensing mechanisms. RIP was tested in the present study for its ability to inhibit S. aureus biofilm formation in a rat Dacron graft model. The activity of RIP was synergistic with those of antibiotics for the complete prevention of drug-resistant S. aureus infections.

L13 ANSWER 7 OF 35 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2003377214 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12885754
TITLE: Prophylactic efficacy of topical temporin A and RNAIII-inhibiting peptide in a subcutaneous rat Pouch model of graft infection attributable to **staphylococci** with intermediate resistance to glycopeptides.
AUTHOR: Cirioni Oscar; Giacometti Andrea; Ghiselli Roberto; Dell'Acqua Giorgio; Gov Yael; Kamysz Wojciech; Lukasiak Jerzy; Mocchegiani Federico; Orlando Fiorenza; D'Amato Giuseppina; **Balaban Naomi**; Saba Vittorio; Scalise Giorgio
CORPORATE SOURCE: Institute of Infectious Diseases and Public Health, University of Ancona, Ancona, Italy.
SOURCE: Circulation, (2003 Aug 12) 108 (6) 767-71. Electronic Publication: 2003-07-28.
Journal code: 0147763. ISSN: 1524-4539.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 20030813
Last Updated on STN: 20030918
Entered Medline: 20030917

ED Entered STN: 20030813
Last Updated on STN: 20030918
Entered Medline: 20030917

AB BACKGROUND: Bacteria that adhere to implanted medical devices play an important role in industry and in modern medicine. **Staphylococci** are among the most common pathogens that cause biomaterial infections. Vascular prosthetic graft infection is one of the most feared complications that the vascular surgeon treats, frequently resulting in prolonged hospitalization, organ failure, amputation, and death. A rat model was used to investigate the topical efficacies of temporin A and the quorum-sensing inhibitor RNAIII-inhibiting protein (RIP) as prophylactic agents of vascular prosthetic graft infections caused by **Staphylococcus** aureus and **Staphylococcus** epidermidis with intermediate resistance to glycopeptides. METHODS AND RESULTS: Graft infections were established in the back subcutaneous tissue of adult male Wistar rats by implantation of Dacron prostheses 1 cm2 followed by topical inoculation with 2x10(7) colony-forming units of bacterial strains. The study included, for each **staphylococcal** strain, a control group (no graft contamination), a contaminated group that did not receive antibiotic prophylaxis, and 6 contaminated groups that received grafts soaked with temporin A, RIP, rifampin, temporin A plus RIP, RIP plus rifampin, or temporin A plus RIP. The infection was evaluated by quantitative agar culture. When tested alone, temporin A and RIP showed comparable efficacies, and their efficacies were significantly higher than that of rifampin against both strains. All combinations showed efficacies

significantly higher than that of each single compound. The combinations of temporin A and RIP exerted the strongest antistaphylococcal efficacies, eliminating infection by 100%. CONCLUSIONS: The results of the present study make these molecules potentially useful for antimicrobial chemoprophylaxis in vascular surgery.

L13 ANSWER 8 OF 35 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2003087147 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12599079
TITLE: Use of the quorum-sensing inhibitor RNAIII-inhibiting peptide to prevent biofilm formation in vivo by drug-resistant **Staphylococcus** epidermidis.
AUTHOR: **Balaban Naomi**; Giacometti Andrea; Cirioni Oscar; Gov Yael; Ghiselli Roberto; Mocchegiani Federico; Viticchi Claudio; Del Prete Maria Simona; Saba Vittorio; Scalise Giorgio; Dell'Acqua Giorgio
CORPORATE SOURCE: Department of Human Microbiology, Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel.. nbalaban@ucdavis.edu
SOURCE: Journal of infectious diseases, (2003 Feb 15) 187 (4) 625-30. Electronic Publication: 2003-02-07. Journal code: 0413675. ISSN: 0022-1899.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200304
ENTRY DATE: Entered STN: 20030225
Last Updated on STN: 20030402
Entered Medline: 20030401
ED Entered STN: 20030225
Last Updated on STN: 20030402
Entered Medline: 20030401
AB **Staphylococcus** epidermidis is a frequent cause of infections associated with foreign bodies and indwelling medical devices. The bacteria are capable of surviving antibiotic treatment through encapsulation into biofilms. RNAIII-inhibiting peptide (RIP) is a heptapeptide that inhibits S. aureus pathogenesis by disrupting quorum-sensing mechanisms. In this study, RIP inhibited drug-resistant S. epidermidis biofilm formation through a mechanism similar to that evidenced for S. aureus. RIP is synergistic with antibiotics in eliminating 100% of graft-associated in vivo S. epidermidis infections, which suggests that RIP may be used to coat medical devices to prevent **staphylococcal** infections. Disruption of cell-cell communication can prevent infections associated with antibiotic-resistant strains.

L13 ANSWER 9 OF 35 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 2003337817 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12472801
TITLE: Prevention of **Staphylococcus** aureus biofilm on dialysis catheters and adherence to human cells.
AUTHOR: **Balaban Naomi**; Gov Yael; Bitler Arkady; Boelaert Johan R
CORPORATE SOURCE: Department of Human Microbiology, Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel.. nbalaban@ucdavis.edu
SOURCE: Kidney international, (2003 Jan) 63 (1) 340-5. Journal code: 0323470. ISSN: 0085-2538.
PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 20030722
Last Updated on STN: 20040303
Entered Medline: 20040302

ED Entered STN: 20030722
Last Updated on STN: 20040303
Entered Medline: 20040302

AB BACKGROUND: Dialysis patients, often carriers of **Staphylococcus** aureus in their nares, are at high risk of S. aureus infections. METHODS: We examined whether RNAIII inhibiting peptide (RIP), which interferes with quorum sensing mechanisms, reduces adherence of S. aureus to host cells and to dialysis catheter polymers in vitro. Adherence was tested by spectroscopy using safranin staining, by confocal scanning laser microscopy and by atomic force microscopy. RESULTS: RIP inhibited bacterial adherence to HaCat and HEp-2 cells and reduced adherence and biofilm formation not only on polystyrene, but also on both polyurethane- and silicone-made dialysis catheters, with a preponderant effect on silicone, to which bacteria were more adherent. CONCLUSION: RIP opens a new perspective in anti-S. aureus prophylaxis, particularly in dialysis patients.

L13 ANSWER 10 OF 35 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 2003301569 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12829282
TITLE: Characterization of RAP, a quorum sensing activator of **Staphylococcus** aureus.
AUTHOR: Korem Moshe; Sheoran Abhineet S; Gov Yael; Tzipori Saul; Borovok Ilya; **Balaban Naomi**
CORPORATE SOURCE: Department of Human Microbiology, Sackler School of Medicine, Tel Aviv University, Israel.
SOURCE: FEMS microbiology letters, (2003 Jun 27) 223 (2) 167-75. Journal code: 7705721. ISSN: 0378-1097.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 20030628
Last Updated on STN: 20030816
Entered Medline: 20030815

ED Entered STN: 20030628
Last Updated on STN: 20030816
Entered Medline: 20030815

AB **Staphylococcus** aureus are Gram-positive bacteria and cause diverse serious diseases in humans and animals through the production of toxins. The production of toxins is regulated by quorum sensing mechanisms, where proteins such as RNAIII activating protein (RAP) are secreted by the bacteria and induce virulence. Antibodies to RAP have been shown to protect mice from infection, but the molecular structure of RAP was not known and hindered vaccine development. To characterize RAP, recombinant protein was made and tested for its ability to induce genes important for pathogenesis (agr). In addition, monoclonal antibodies were produced to identify its cellular localization. Results shown here indicate that RAP is a 277-aa protein that is an ortholog of the ribosomal protein L2. Like the native molecule, recombinant RAP activates the production of RNAIII (encoded by agr). Using RAP specific monoclonal

antibodies we demonstrate that RAP is continuously secreted and while RAP is expressed also in other bacteria (like **Staphylococcus** epidermidis, **Staphylococcus** xylosus and Escherichia coli), it is secreted to the culture medium only by S. aureus. Our results show that the ribosomal protein L2 has an extraribosomal function and that when secreted RAP acts as an autoinducer of virulence to regulate S. aureus pathogenesis.

L13 ANSWER 11 OF 35 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 2001286612 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11160124
TITLE: Regulation of **Staphylococcus** aureus pathogenesis via target of RNAIII-activating Protein (TRAP).
COMMENT: Erratum in: J Biol Chem 2001 Apr 13;276(15):12476
Erratum in: J Biol Chem 2001 Jun 8;276(23):20803
AUTHOR: **Balaban N**; Goldkorn T; Gov Y; Hirshberg M; Koyfman N; Matthews H R; Nhan R T; Singh B; Uziel O
CORPORATE SOURCE: Departments of Pathology, Internal Medicine, and Biological Chemistry, University of California, Davis 95616, USA.. nbalaban@ucdavis.edu
SOURCE: Journal of biological chemistry, (2001 Jan 26) 276 (4) 2658-67.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF202641
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010625
Last Updated on STN: 20010723
Entered Medline: 20010621
ED Entered STN: 20010625
Last Updated on STN: 20010723
Entered Medline: 20010621
AB **Staphylococcus** aureus can cause disease through the production of toxins. Toxin production is autoinduced by the protein RNAIII-activating protein (RAP) and by the autoinducing peptide (AIP), and is inhibited by RNAIII-inhibiting peptide (RIP) and by inhibitory AIPs. RAP has been shown to be a useful vaccine target site, and RIP and inhibitory AIPs as therapeutic molecules to prevent and suppress S. aureus infections. Development of therapeutic strategies based on these molecules has been hindered by a lack of knowledge of the molecular mechanisms by which they activate or inhibit virulence. Here, we show that RAP specifically induces the phosphorylation of a novel 21-kDa protein, whereas RIP inhibits its phosphorylation. This protein was termed target of RAP (TRAP). The synthesis of the virulence regulatory molecule, RNAIII, is not activated by RAP in the trap mutant strain, suggesting that RAP activates RNAIII synthesis via TRAP. Phosphoamino acid analysis shows that TRAP is histidine-phosphorylated, suggesting that TRAP may be a sensor of RAP. AIPs up-regulate the synthesis of RNAIII also in trap mutant strains, suggesting that TRAP and AIPs activate RNAIII synthesis via distinct signal transduction pathways. Furthermore, TRAP phosphorylation is down-regulated in the presence of AIP, suggesting that a network of signal transduction pathways regulate S. aureus pathogenesis.

L13 ANSWER 12 OF 35 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 2001541408 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11587789

TITLE: RNAIII inhibiting peptide (RIP), a global inhibitor of **Staphylococcus** aureus pathogenesis: structure and function analysis.
AUTHOR: Gov Y; Bitler A; Dell'Acqua G; Torres J V; **Balaban N**
CORPORATE SOURCE: Department of Human Microbiology, Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel.
SOURCE: Peptides, (2001 Oct) 22 (10) 1609-20.
Journal code: 8008690. ISSN: 0196-9781.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011008
Last Updated on STN: 20020122
Entered Medline: 20011214

ED Entered STN: 20011008
Last Updated on STN: 20020122
Entered Medline: 20011214

AB **Staphylococcus** aureus are gram-positive bacteria that can cause serious diseases in humans and animals. S. aureus infections can be prevented by the heptapeptide RNAIII inhibiting peptide (RIP). RIP was originally isolated from culture supernatants of coagulase negative **staphylococci** presumed to be S. xylosus. The sequence of RIP was identified as YSPXTNF. Native RIP and its synthetic analogue YSPWTNF have been shown to be effective inhibitors of diseases caused by various strains of S. aureus, including, cellulitis, keratitis, septic arthritis, osteomylitis and mastitis. RIP is therefore considered to be a global inhibitor of S. aureus. We show here that: 1) the amide form of RIP (YSPWTNF-NH2) is highly stable and is therefore the one recommended for use. 2) RIP inhibits S. aureus pathogenesis by inhibiting the synthesis of both agr transcripts RNAII and RNAIII. 3) Although RIP inhibits agr, it also reduces bacterial adherence to mammalian cells and to plastic (tested on HEp2 cells and on polystyrene by fluorescence and atomic force microscopy), suggesting that RIP can be used safely as a therapeutic molecule. 4) RIP derivatives were designed and tested for their ability to inhibit RNAIII in vitro and cellulitis in vivo. Not all peptides that inhibited RNAIII also inhibited an infection in vivo, indicating that studies must be carried out in vivo before considering a peptide to be of therapeutic potential. 5) The RIP derivative containing Lysine and Isoleucine at positions 2 and 4, respectively, inhibited S. aureus infections in vivo (tested on cellulitis), suggesting that both RIP YSPWTNF and its derivative YKPITNF are effective inhibitors of infections caused by S. aureus.

L13 ANSWER 13 OF 35 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 2001558771 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11252509
TITLE: Analytical chromatography for recovery of small amounts of **staphylococcal** enterotoxins from food.
AUTHOR: **Balaban N**; Rasooly A
CORPORATE SOURCE: Department of Medical Pathology, University of California, Davis 95616, USA.
SOURCE: International journal of food microbiology, (2001 Feb 28) 64 (1-2) 33-40.
Journal code: 8412849. ISSN: 0168-1605.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20011022
Last Updated on STN: 20011022
Entered Medline: 20011018

ED Entered STN: 20011022
Last Updated on STN: 20011022
Entered Medline: 20011018

AB Sample preparation is an important element in the detection of toxins in food samples. In this work, a simple analytical sample preparation method for recovery of small amount of **staphylococcal** enterotoxin B (SEB) and **staphylococcal** enterotoxin A (SEA) in food samples was developed. Cation exchanger carboxymethylcellulose (CM) was used for small-scale batch chromatography isolation of SEB from infant formula and from mushrooms spiked with SEB. The resulting materials were analyzed for SEB by Western immunoblotting. Nearly all of the extraneous substances in the sample were removed by this procedure with no significant loss of the toxin. Using this method, even small amounts of SE (0.75 ng/g) can be recovered and immunologically analyzed by Western blotting or by ELISA with a very low background. Because this method is effective, rapid, simple and inexpensive, it has the potential to be a general method for the preparation of samples used for analysis of SEs.

L13 ANSWER 14 OF 35 MEDLINE on STN DUPLICATE 14
ACCESSION NUMBER: 2001075018 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11072116
TITLE: Prevention of diseases caused by **Staphylococcus** aureus using the peptide RIP.
AUTHOR: **Balaban N**; Collins L V; Cullor J S; Hume E B; Medina-Acosta E; Vieira da Motta O; O'Callaghan R; Rossitto P V; Shirtliff M E; Serafim da Silveira L; Tarkowski A; Torres J V
CORPORATE SOURCE: Department of Medical Pathology, University of California, Davis 95616, USA.. nbalaban@ucdavis.edu
SOURCE: Peptides, (2000 Sep) 21 (9) 1301-11.
Journal code: 8008690. ISSN: 0196-9781.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010104

ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010104

AB **Staphylococcus** aureus causes many diseases including cellulitis, keratitis, osteomyelitis, septic arthritis and mastitis. The heptapeptide RIP has been shown to prevent cellulitis in mice, which was induced by S. aureus strain Smith diffuse. Here we show that RIP can also significantly reduce the overall pathology and delay the onset of disease symptoms in several other models of S. aureus infections, including: keratitis (tested in rabbits against S. aureus 8325-4), osteomyelitis (tested in rabbits against S. aureus MS), mastitis (tested in cows against S. aureus Newbould 305, AE-1, and environmental infections) and septic arthritis (tested in mice against S. aureus LS-1). These findings substantiate that RIP is not strain specific in its inhibitory activity and that RIP is an effective

inhibitor of bacterial pathology at multiple body sites following diverse routes and doses of administration. These findings strongly evidence the potential value of RIP as a chemotherapeutic agent.

L13 ANSWER 15 OF 35 MEDLINE on STN DUPLICATE 15
ACCESSION NUMBER: 2000477584 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11028954
TITLE: **Staphylococcal** enterotoxins.
AUTHOR: **Balaban N**; Rasooly A
CORPORATE SOURCE: Department of Medical Pathology, University of California, Davis 95616, USA.
SOURCE: International journal of food microbiology, (2000 Oct 1) 61 (1) 1-10. Ref: 84
Journal code: 8412849. ISSN: 0168-1605.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010215
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010215
AB **Staphylococcus** aureus is a major human pathogen that produces a wide array of toxins, thus causing various types of disease symptoms. **Staphylococcal** enterotoxins (SEs), a family of nine major serological types of heat stable enterotoxins, are a leading cause of gastroenteritis resulting from consumption of contaminated food. In addition, SEs are powerful superantigens that stimulate non-specific T-cell proliferation. SEs share close phylogenetic relationships, with similar structures and activities. Here we review the structure and function of each known enterotoxin.

L13 ANSWER 16 OF 35 MEDLINE on STN DUPLICATE 16
ACCESSION NUMBER: 1998212065 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9545222
TITLE: Autoinducer of virulence as a target for vaccine and therapy against **Staphylococcus** aureus.
COMMENT: Comment in: Science. 1998 Apr 17;280(5362):379. PubMed ID: 9575082
Comment in: Science. 2000 Jan 21;287(5452):391
AUTHOR: **Balaban N**; Goldkorn T; Nhan R T; Dang L B; Scott S; Ridgley R M; Rasooly A; Wright S C; Larrick J W; Rasooly R; Carlson J R
CORPORATE SOURCE: Department of Medical Pathology, University of California, Davis, CA 95616, USA.. nbalaban@ucdavis.edu
CONTRACT NUMBER: AI40830 (NIAID)
SOURCE: Science, (1998 Apr 17) 280 (5362) 438-40.
Journal code: 0404511. ISSN: 0036-8075.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 19980514

Last Updated on STN: 20000218
Entered Medline: 19980507

ED Entered STN: 19980514
Last Updated on STN: 20000218
Entered Medline: 19980507

AB **Staphylococcus** aureus causes pathologies ranging from minor skin infections to life-threatening diseases. Pathogenic effects are largely due to production of bacterial toxin, which is regulated by an RNA molecule, RNAIII. The S. aureus protein called RAP (RNAIII activating protein) activates RNAIII, and a peptide called RIP (RNAIII inhibiting peptide), produced by a nonpathogenic bacteria, inhibits RNAIII. Mice vaccinated with RAP or treated with purified or synthetic RIP were protected from S. aureus pathology. Thus, these two molecules may provide useful approaches for the prevention and treatment of diseases caused by S. aureus.

L13 ANSWER 17 OF 35 MEDLINE on STN DUPLICATE 17
ACCESSION NUMBER: 95183517 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7533297
TITLE: Autocrine regulation of toxin synthesis by **Staphylococcus** aureus.
AUTHOR: **Balaban N**; Novick R P
CORPORATE SOURCE: Skirball Institute, New York University Medical Center, NY 10016.
CONTRACT NUMBER: RO1 AI30138 (NIAID)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (1995 Feb 28) 92 (5) 1619-23. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199504
ENTRY DATE: Entered STN: 19950419
Last Updated on STN: 19960129
Entered Medline: 19950404

ED Entered STN: 19950419
Last Updated on STN: 19960129
Entered Medline: 19950404

AB **Staphylococcus** aureus is a major human pathogen causing diseases which range from minor skin infection to endocarditis and toxic shock syndrome. The pathogenesis of S. aureus is due primarily to the production of toxic exoproteins, whose synthesis is controlled by a global regulatory system, agr. We show here that agr is autoinduced by a proteinaceous factor produced and secreted by the bacteria and that it is inhibited by a peptide produced by an exoprotein-deficient S. aureus mutant strain. The inhibitor, RIP, competes with the activator, RAP, and may be a mutational derivative. Our results suggest two possible approaches, independent of antibiotics, to the control of S. aureus infections. RIP may prove useful as a direct inhibitor of virulence and RAP as a vaccine against the expression of agr-induced virulence factors; either could interfere with the ability of the bacteria to establish and maintain an infection.

L13 ANSWER 18 OF 35 MEDLINE on STN DUPLICATE 18
ACCESSION NUMBER: 96079506 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8566701
TITLE: Translation of RNAIII, the **Staphylococcus** aureus agr regulatory RNA molecule, can be activated by a 3'-end

deletion.
AUTHOR: **Balaban N**; Novick R P
CORPORATE SOURCE: California Regional Primate Research Center, University of California, Davis 95616, USA.
CONTRACT NUMBER: R01-A130138
SOURCE: FEMS microbiology letters, (1995 Nov 1) 133 (1-2) 155-61. Journal code: 7705721. ISSN: 0378-1097.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199603
ENTRY DATE: Entered STN: 19960315
Last Updated on STN: 19960315
Entered Medline: 19960301
ED Entered STN: 19960315
Last Updated on STN: 19960315
Entered Medline: 19960301
AB RNAIII, an RNA molecule shown to encode delta-hemolysin and independently to regulate toxin synthesis in **Staphylococcus** aureus, is transcribed at the mid-exponential phase of growth, while its target genes are activated 2 h later, at the post-exponential phase of growth. We show here that the translation of RNAIII to the 26-amino acid peptide delta-hemolysin is delayed by 1 h, and that this delay is abolished when the 3'-end of this molecule is deleted. We suggest that structural changes of RNAIII to a translatable form of the molecule precede its regulation of target gene expression.

L13 ANSWER 19 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:104508 CAPLUS
TITLE: Genotype distribution of Candida albicans isolates by 25S intron analysis with regard to invasiveness
AUTHOR(S): Karahan, Z. C.; Gueriz, H.; Agirbasli, H.; **Balaban**, **N**.; Goecmen, J. S.; Aysev, D.; Akar, N.
CORPORATE SOURCE: Division of Pediatric Molecular Pathology and Genetics, Faculty of Medicine, Ankara University, Ankara, Turk.
SOURCE: Mycoses (2004), 47(11-12), 465-469
CODEN: MYCSEU; ISSN: 0933-7407
PUBLISHER: Blackwell Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 07 Feb 2005
AB The aim of this study was to genotype Candida albicans strains isolated from patients with invasive and non-invasive deep-seated infections. For this purpose, 301 C. albicans isolates (81 invasive and 220 non-invasive) were genotyped by using specific PCR primers designed to span the transposable group I intron of the 25S rDNA gene. Fifty-three of the 81 invasive isolates were genotype A (65.4%), eight were genotype B (9.9%) and 20 were genotype C (24.7%), while 98 of the 220 non-invasive isolates were genotype A (44.6%), 46 were genotype B (20.9%) and 76 were genotype C (34.5%). Genotype A was more prevalent among invasive isolates and genotypes B and C were more prevalent among non-invasive isolates ($P = 0.0046$). Genotypes D and E which represent C. dubliniensis were not found. These results indicate that there may be a relationship between C. albicans genotypes and invasiveness; genotype A being more invasive than others. The presence or absence of the transposable group I intron in the 25S rDNA gene may be important in determining the invasiveness of C. albicans.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 20 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:603706 CAPLUS
DOCUMENT NUMBER: 139:349264
TITLE: Antioxidant activity of seminal plasma in fertile and infertile men
AUTHOR(S): Koca, Y.; Oezdal, Oe. L.; Celik, M.; Uenal, S.; **Balaban, N.**
CORPORATE SOURCE: Department of Biochemistry, Ankara Numune Education and Research Hospital, Ankara, Turk.
SOURCE: Archives of Andrology (2003), 49(5), 355-359
CODEN: ARANDR; ISSN: 0148-5016
PUBLISHER: Taylor & Francis, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 06 Aug 2003
AB This study was conducted to evaluate and compare the total antioxidant capacity among fertile and infertile men. Thirty infertile patients and 20 fertility-proven healthy donors with normal sperm anal. were included in the study. Total antioxidant capacity, zinc and fructose levels of seminal plasma, and various sperm parameters were compared among fertile controls and idiopathic infertility patients prospectively. The mean antioxidant capacity of fertile controls (2.02±0.16 mmol/L) was significantly higher than that of the infertile patients group (1.78±0.23 mmol/L) ($p<.01$). Furthermore, asthenozoospermic and asthenoteratozoospermic groups had significantly lower mean antioxidant values (1.73±0.11 and 1.64±0.13, resp.) when compared to fertile control group ($p<.01$). The mean fructose level was significantly lower in the fertile control group and mean zinc level was significantly lower in the entire infertile group. On the other hand, antioxidant capacity is pos. correlated to sperm motility ($p=.001$). Decreased antioxidant capacity was associated with impaired sperm function as a result of either increased ROS production or insufficient antioxidant capacity.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 21 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:720315 CAPLUS
TITLE: Peptides: bacteria's point of view
AUTHOR(S): **Balaban, N.**; Koyfman, N.
CORPORATE SOURCE: Sackler School of Medicine, Department of Human Microbiology, Tel Aviv University, Tel Aviv-Jaffa, Israel
SOURCE: Peptides (New York, NY, United States) (2001), 22(10), 1517-1518
CODEN: PPTDD5; ISSN: 0196-9781
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal; Miscellaneous
LANGUAGE: English
ED Entered STN: 03 Oct 2001
AB Unavailable

L13 ANSWER 22 OF 35 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:475214 CAPLUS
DOCUMENT NUMBER: 136:213089
TITLE: Comparison of different methods used in the diagnosis of Clostridium difficile associated infections

molecular weight of 21 kDa, and is obtained from a Staphylococcus bacteria. INDEPENDENT CLAIMS are also included for the following:

(1) an isolated nucleic acid molecule (NAM) (II) consisting of a coding sequence for (I);

(2) an antibody immunoreactive with TRAP;

(3) a device (e.g. a catheter, a needle, a surgical instrument, and a tampon) comprising a surface coating composition comprising a TRAP inhibitor;

(4) a vaccine comprising TRAP; and

(5) identifying biologically active agents that modulate TRAP activity, comprising combining a candidate agent with TRAP and RAP, and detecting (by detecting of TRAP phosphorylation or by detecting production of RNAIII) the inhibition of TRAP activity in production of Staphylococcus virulence factors;

(6) treating Staphylococcus bacteria, comprising administering to a patient a therapeutically effective amount of a TRAP inhibitory agent (e.g. an anti- TRAP antibody); and

(7) preventing S. aureus infection, comprising administering to a subject a compound which generates an immune response thereby creating antibodies which bind RAP.

ACTIVITY - Antibacterial. No biological data given.

MECHANISM OF ACTION - Vaccine. No biological data given.

USE - The target RNAIII activating protein (TRAP) DNA sequences may be used as probes for identifying TRAP coding sequences of other strains of Staphylococcus or other bacteria. They may also be used to detect the TRAP nucleic acids in biological samples, and to produce the polypeptide recombinantly. The polypeptides are used to raise antibodies, and in assays to identify inhibitory compounds (claimed) which are then used to treat Staphylococcal infections. The TRAP polypeptides may be used for vaccination (claimed). Agents which inhibit the expression of TRAP or which inhibit its activity are candidates for the development of treatments for infection of pathogenic Staphylococcus. The pharmaceutical formulations are used for suppressing the production of toxins by a Staphylococcus bacteria, especially S. aureus.

ADVANTAGE - None given.

DESCRIPTION OF DRAWING(S) - The figure is a simplified diagram summarizing the role of target RNAIII activating protein (TRAP), RNAIII activating protein (RAP), and RNAIII in the production of toxins in Staphylococcus.

Dwg.1/17

ABEX UPTX: 20000516

ADMINISTRATION - Human dosage levels are a daily dose of 0.1-500 mg/kg body weight, preferably 6-200 mg/kg, and especially 12-100 mg/kg.

EXAMPLE - In vivo phosphorylation assays were carried out using wild type target RNAIII activating protein (TRAP) polypeptides. Wild type early exponential S. aureus cells were incubated for 1 hour in phosphate free buffer (PFB) together with 32P, with RNAIII activating protein (RAP) in phosphate buffered saline (PBS), or with only PBS as a control. After 1 hours, cells were collected, and applied to a SDS-PAGE gel, and the gel electrophoresed and autoradiographed. The autoradiogram was scanned and the density of the bands determined. The results show that RAP causes the specific phosphorylation of TRAP.

L13 ANSWER 34 OF 35 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 1999-405112 [34] WPIX
CROSS REFERENCE: 2005-123072 [13]
DOC. NO. CPI: C1999-119587
TITLE: RNAIII activating protein antagonist.

DERWENT CLASS: B04 D16
INVENTOR(S): **BALABAN, N**; LARRICK, J W; WRIGHT, S C
PATENT ASSIGNEE(S): (PANO-N) PANORAMA RES INC; (REGC) UNIV CALIFORNIA; (BALA-I) BALABAN N; (PANO-N) PANORAMA RES
COUNTRY COUNT: 85
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9932133	A1	19990701	(199934)*	EN	33
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW					
AU 9920050	A	19990712	(199950)		
EP 1037650	A1	20000927	(200048)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
US 6291431	B1	20010918	(200157)		
US 2004072748	A1	20040415	(200426)		
US 2004077534	A1	20040422	(200428)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9932133	A1		WO 1998-US27091	19981218
AU 9920050	A		AU 1999-20050	19981218
EP 1037650	A1		EP 1998-964810	19981218
			WO 1998-US27091	19981218
US 6291431	B1	Provisional	US 1997-68094P	19971219
			US 1998-54331	19980402
US 2004072748	A1	Provisional	US 1997-68094P	19971219
		CIP of	US 1998-54331	19980402
		CIP of	US 2001-839695	20010419
			US 2003-358448	20030203
US 2004077534	A1	Provisional	US 1997-68094P	19971219
		CIP of	US 1998-54331	19980402
			US 2001-839695	20010419

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9920050	A	Based on	WO 9932133
EP 1037650	A1	Based on	WO 9932133
US 2004072748	A1	CIP of	US 6291431
US 2004077534	A1	CIP of	US 6291431

PRIORITY APPLN. INFO: US 1998-54331 19980402; US 1997-68094P 19971219; US 2001-839695 20010419; US 2003-358448 20030203

AB WO 9932133 A UPAB: 20050224
NOVELTY - RNAIII activating protein (RAP) antagonist (I) is new.
DETAILED DESCRIPTION - A composition comprising a polypeptide comprising an amino acid sequence of general formula (I) is new:
Y(K/S)PXTNF (I)

X = C, W or I

INDEPENDENT CLAIMS are also included for the following:

(1) a composition comprising a nucleic acid molecule encoding a polypeptide as above; and

(2) a composition comprising an antibody which specifically binds to the polypeptide above.

ACTIVITY - Antibacterial; Immunoprotective.

MECHANISM OF ACTION - RAP Antagonist.

USE - A peptide, termed RNAIII inhibiting peptide (RIP) is produced by a non-pathogenic strain of Staphylococcus aureus mutated by nitrosoguanidine. RIP competes with RAP for the activation of RNAIII, and thus inhibits toxin production by S. aureus. The polypeptide composition is useful for treating a host for staphylococcal infection (claimed). A RAP receptor antagonist, e.g. a polypeptide, peptidomimetic or antibody can be used to treat staphylococcal infection (claimed). Antibodies can be screened for the ability to block the binding of a ligand to RAP or RIP and/or for other properties, e.g. the ability to protect in vivo against S. aureus infection.

Dwg.0/5

ABEX UPTX: 19990825

ADMINSTRATION - The composition is administered after onset of symptoms or prophylactically (claimed).

EXAMPLE - Purified and synthetic RIP were tested for their ability to suppress infection in the murine cutaneous Staphylococcus aureus infection model. Smith Diffuse S. aureus (8.5 x 107 - 1.4 x 109) were incubated in the presence of RIP which was purified from 5 ml postexponential culture broth of ATCC 55619 in saline, or with saline only as a control, with 0.5 mg synthetic RIP (Pep) in a final DMSO (in saline) solution of 3%, or only with 3 % DMSO in saline as a control for 30 minutes at 37degreesC. The bacteria + RIP, bacteria + Pep, bacteria + saline or bacteria + DMSO mixture was injected subcutaneously together with cytodex beads (1 mg) into 8 week old male hairless immunocompetent mice to induce a local infection. The size of the lesion was measured daily. For these experiments mice were pre-screened to eliminate individuals with anti-RAP antibodies. A fixed amount of RIP (approximately10 mg) attenuated infections caused by increasing inocula of the Smith Diffuse strain of S. aureus. Of the animals that were injected with 8.5 x 107 bacteria together with RIP, three of four developed no infection at all, as compared to only one of four control animals that were injected with the bacteria and saline. When an increased inoculum of bacteria was used (1.4 x 108 cells per injection) 4/8 animals were protected, whereas the remaining four developed a lesion that was 55% smaller than that of control animals. All (7/7) of the control animals challenged with SD and saline developed a lesion. When a higher number of bacteria was used (1.4 x 109) the synthetic RIP (0.5 mg Pep) protected animals, where 90% (9/10) of the animals showed no sign of disease.

L13 ANSWER 35 OF 35 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
ACCESSION NUMBER: 1996-209319 [21] WPIX
CROSS REFERENCE: 1998-018426 [02]; 2003-074097 [07]; 2003-606005 [57]
DOC. NO. CPI: C1996-066766
TITLE: Peptide that inhibits expression of virulence factors in Staphylococcus aureus - useful for treating or preventing Staph. aureus infections, partic. in immuno compromised patients, and in vaccines when coupled to immunogen.
DERWENT CLASS: B04 D16
INVENTOR(S): **BALABAN**, **N**; JI, G; NOVICK, R P
PATENT ASSIGNEE(S): (UYNY) UNIV NEW YORK STATE
COUNTRY COUNT: 19

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9610579	A1	19960411	(199621)*	EN	44
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE					
W: AU CA JP					
AU 9538259	A	19960426	(199631)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9610579	A1	WO 1995-US12708	19951002
AU 9538259	A	AU 1995-38259	19951002

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9538259	A	Based on	WO 9610579

PRIORITY APPLN. INFO: US 1994-318499 19941004

AB WO 9610579 A UPAB: 20030906

Peptide (I) that inhibits agr-rnaIII transcription in Staphylococcus aureus is new. Also claimed are: (1) a peptide (II) that activates agr-rnaIII transcription in S. aureus; (2) an antibody (Ab1) that binds specifically to (II); (3) purified, isolated protein (III) with same activity as (II); and(4) antibodies (Ab2) that are immunoreactive with (III).

USE - (I), Ab1 and Ab2 can be used to block the expression of virulence factors produced by S. aureus, i.e. to treat or prevent S. aureus infections, partic. in immunocompromised patients. (II) and (III), when coupled to a suitable immunogen, can also be used in preventive vaccines.

Dwg.0/11

=> file home
FILE 'HOME' ENTERED AT 14:56:41 ON 16 JUN 2005

=>